Amendments to the Specification:

Please replace Table 3 beginning at p. 27, line 28 with the following marked up replacement paragraph

Table 3

N-terminal Sequences and Amounts of ß-secretase Forms in Various Cell Types

Source	Est. Amount (pmoles)	N-terminus (Ref.: SEQ ID NO: 2)	Sequence
Human brain	1-2	46	ETDEEPEEPGR... (SEQ ID NO:76)
Recombinant, 293T	~35	46	ETDEEPEEPGR... (SEQ ID NO:76)
	~7	22	TQHGIRL(P)LR... (SEQ ID NO:77)
	~5	63	MVDNLRGKS... (SEQ ID NO:78)
Recombinant, CosA2	~4	46	ETDEEPEEPGR... (SEQ ID NO:76)
	~3	58	GSFVEMVDNL... (SEQ ID NO:79)

Please replace the paragraph beginning at p. 35, line 26 with the following marked up replacement paragraph

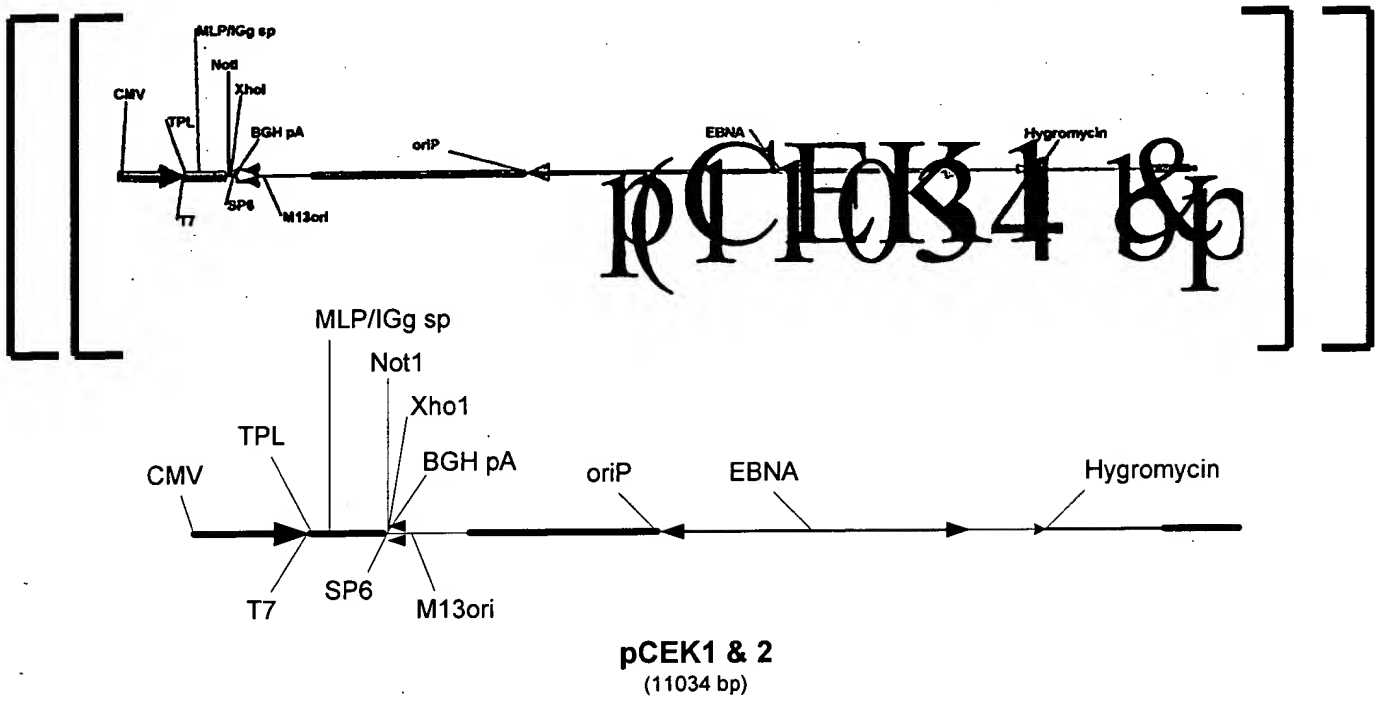
CTGTTGGGCTCGCGGTTGAGGACAAACTCTTCGCGGTCTTTCCAGTACTCTTG
GATCGGAAACCCGTCGGCCTCCGAACGGTACTCCGCCACCGAGGGACCTGAG
CGAGTCCGCATCGACCGGATCGGAAAACCTCTCGACTGTTGGGGTGAGTACT
CCCTCTCAAAAGCGGGCATGACTTCTGCGCTAAGATTGTCAGTTTCCAAAAAC
GAGGAGGATTTGATATTCACCTGGCCCGCGGTGATGCCTTTGAGGGTGGCCG
CGTCCATCTGGTCAGAAAAGACAATCTTTTTGTTGTCAAGCTTGAGGTGTGGC
AGGCTTGAGATCTGGCCATACACTTGAGTGACAATGACATCCACTTTGCCTTT
CTFTCCACAGGTGTCCACTCCCAGGTCCAACTGCAGGTCGACTCTAGACCC (SEQ ID NO:80)

Please replace the paragraph beginning at p. 63, line 18 with the following marked up replacement paragraph

Poly A+ RNA from IMR human neuroblastoma cells was reverse transcribed using the Perkin-Elmer kit. Eight degenerate primer pools, each 8 fold degenerate, encoding the N and C terminal portions of the amino acid sequence obtained from the purified protein were designed (shown in Table 6; oligos 3407 through 3422). PCR reactions were composed of cDNA from 10 ng of RNA, 1.5 mM $MgCl_2$, 0.125 µl AmpliTaq® Gold, 160 µM each dNTP (plus 20µM additional from the reverse transcriptase reaction), Perkin-Elmer TAQ buffer (from AmpliTaq® Gold kit, Perkin-Elmer, Foster City, CA), in a 25 µl reaction volume. Each of oligonucleotide primers 3407 through 3414 was used in combination with each of oligos 3415 through 3422 for a total for 64 reactions. Reactions were run on the Perkin-Elmer 7700 Sequence Detection machine under the following conditions: 10 min at 95°C, 4 cycles of, 45° C annealing for 15 second, 72° C extension for 45 second and 95°C denaturation for 15 seconds followed by 35 cycles under the same conditions with the exception that the annealing temperature was raised to 55° C . (The foregoing conditions are referred to herein as "Reaction 1 conditions.") PCR products were visualized on 4% agarose gel (Northern blots) and a prominent band of the expected size (68 bp) was seen in reactions, particularly with the primers 3515-3518 in many of the lanes (each of FIGS 3A-3C shows two gels, an upper and a lower gel, and the reaction combinations were run sequentially in the gels as illustrated, such that primer 3515 was reacted with each of 3507-3514, followed by reaction of primer 3516 with each of primers 3507-3514, and so forth). The 68 kb band was sequenced and the internal region coded for the expected amino acid sequence. This gave the exact DNA sequence for 22 bp of the internal region of this fragment.
C.GGC.CGG.AGG.GGC.AGC.TTT.GTG (SEQ ID NO:81)

Please replace the paragraph beginning at p. 65, line 9 with the following marked up replacement paragraph

A human primary neuronal cell library in the mammalian expression vector pCEK2 vector was generated using size selected cDNA, and pools of clones generated from different sized inserts. The cDNA library for ß-secretase screening was made with poly(A)$^+$ RNA isolated from primary human neuronal cells. The cloning vector was pCEK2 (map shown below).



Please replace the paragraph beginning at p. 66, line 8 with the following marked up replacement paragraph

Clones from the 1.5 kb pool were screened using a radiolabeled probe generated from a 390 b.p. PCR product generated from clone 9C7E.35. For generation of a probe, PCR product was generated using 3458 and 3468 as primers and clone 9C7E.35 (30 ng) as substrate.

3468: CAG.CAT.AGG.CCA.GCC.CCA.GGA.TGC.CT (SEQ ID NO:82)

3458: GAG GGG CAG CTT TGT GGA GA (SEQ ID NO:83)

Please replace the paragraph beginning at p. 73, line 10 with the following marked up replacement paragraph

Recombinant proteins were generated with both the wild-type APP sequence (MBP-C125 WT) at the cleavage site (..Val-Lys-Met-Asp-Ala..)(SEQ ID NO:84) or the "Swedish" double mutation (MBP-C125 SW) (..Val-Asn-Leu-Asp-Ala..)(SEQ ID NO:85). As shown in FIG. 19, cleavage of the intact MBP-fusion protein results in the generation of a truncated amino-terminal fragment, with the new SW-192 Ab-positive epitope uncovered at the carboxy terminus. This amino-terminal fragment can be recognized on Western blots with the same Ab, or, quantitatively, using an anti-MBP capture-biotinylated SW-192 reporter sandwich format, as shown in FIG. 19.

Please replace the paragraph beginning at p. 82, line 10 with the following marked up replacement paragraph

After the sequential addition of all fourteen residues the P10-P4'sta(D->V) peptide has the sequence NH_2-KTEEISEVN[sta]VAEF-COOH (SEQ ID NO:86), where "sta" represents a statine moiety. The side chain protected peptide resin was deprotected and cleaved from the resin by reacting with anhydrous hydrogen fluoride (HF) at 0°C for one hour. This generated the fully deprotected crude peptide as a C-terminal carboxylic acid.

Please replace the substitute sequence listing filed June 21, 2004 with the paper copy of the second substitute sequence listing enclosed herewith.